REMARKS

Claims 1, 10, 16, 17, 20-24, 31, 32, and 45-65 and 67-69 are pending and claims 10, 16, 18-19, 20-21, 25-30, 33-44, 57, and 66 are canceled.

35 U.S.C. § 112 Rejection

Reconsideration is respectfully requested of the rejection of claims 1, 10, 16, 17, 20-24, 31, 32, 45-65, and 67-69 as not satisfying the enablement requirement of the first paragraph of 35 U.S.C. § 112. The Office asserts that while oral pharmaceutical compositions comprising core-shell particles where the shell is crosslinked are enabled, the specification "does not reasonably provide enablement for a shell component comprising a polymer having permeability for potassium ion that is higher than the permeability for a competing cation."[1] Without conceding to the propriety of the rejection and to expedite prosecution, claim 1 is amended and is directed to an oral or rectal pharmaceutical composition comprising a pharmaceutically acceptable excipient and core-shell particles. These core-shell particles comprise a core component and a shell component; the core component comprises a potassium-binding cation exchange polymer and the shell component comprises a crosslinked polymer produced by free radical polymerization of an ethylenic monomer selected from the group consisting of acrylic, methacrylic, styrenic, dienic, vinylic and combinations thereof. The shell component is essentially not disintegrated during residence and passage through the gastro-intestinal tract of an animal subject.

Thus, amended claim 1 does not require the element of "a shell polymer having permeability for potassium ion that is higher than the permeability for a competing cation." Further, amended claim 1 requires a core of a potassium-binding cation exchange polymer and a shell component of a crosslinked polymer produced by free radical polymerization of an ethylenic monomer selected from the group consisting of acrylic, methacrylic, styrenic, dienic, vinylic and combinations thereof. The core polymers are described in paragraphs [0056] and [0057] and the shell polymers and shell deposition methods are described in paragraphs [0039]

[1] See page 2 of Office action dated March 5, 2009.

and [0040]. Accordingly, the specification would have enabled a skilled person to make and use the core-shell compositions of claim 1.

Further, without conceding to the propriety of the rejection, claim 45 is amended to delete the requirement that the shell polymer have "a permeability for potassium ion that is higher than a permeability for a competing cation" and to add the requirement that the shell polymer be "produced by free radical polymerization of an ethylenic monomer." Thus, claim 45 satisfies the enablement requirement of the first paragraph of 35 U.S.C. § 112 for at least the same reasons as claim 1. Also, claim 68 is amended and like claim 1 does not require the element of "a shell polymer having permeability for potassium ion that is higher than the permeability for a competing cation." Thus, claim 68 satisfies the enablement requirement of the first paragraph of 35 U.S.C. § 112 for at least the same reasons as claim 1. Claims 10, 16, 17, 20-24, 31, 32, 46-65, 67 and 69 are directly or indirectly dependent from claims 1, 45, and 68 and satisfy the enablement requirement of the first paragraph of 35 U.S.C. § 112 for at least the same reasons as claims 1, 45, and 68.

Although the amendment after final Office action was entered, the Office did not provide reasons why amended claims 1, 45, and 68 fail to satisfy the enablement requirement under 35 U.S.C. § 112, paragraph 1. As noted above, the claim language on which the enablement rejection was based was deleted from these claims and the enablement rejection should have been overcome by the deletion of the claim language. Further, the final Office action only included an analysis of undue experimentation and the *Wands* factors, yet stated at the end of the analysis and in the Advisory action that the specification does not satisfy the written description requirement. Because undue experimentation and the *Wands* factors relate to enablement and not written description, it is unclear to applicants what evidence the Office relies on as the basis of the written description rejection.

Reconsideration is requested of the rejection of claim 69 as being indefinite under the second paragraph of 35 U.S.C. § 112. Claim 69 was amended to delete the "solution" form of the composition. Thus, claim 69 satisfies the definiteness requirement of the second paragraph of 35 U.S.C. § 112. Again, although the amendment after final Office action was entered, no reasons were provided as to why amended claim 69 fails to satisfy the definiteness requirement of the second paragraph of 35 U.S.C. § 112.

35 U.S.C. § 102 Rejection

Reconsideration is respectfully requested of the rejection of claims 1, 10, 16, 17, 20, 21, 23, 31, 32, 46-50, 54, 57-63, and 69 as anticipated by Notenbomer (EP 0 730 494) under 35 U.S.C. § 102(b). The Office asserts that although "the product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself." Claim 1 is described above in connection with the 35 U.S.C. § 112 rejection and requires the shell be a "crosslinked polymer produced by free radical polymerization of an ethylenic monomer selected from the group consisting of acrylic, methacrylic, styrenic, dienic, vinylic and combinations thereof." In interpreting this claim element, a skilled person would have known that the crosslinked shell polymer would have had repeat units derived from polymerization of acrylic, methacrylic, styrenic, dienic, or vinylic monomers, or a combination thereof.

Notenbomer generally discloses methods and particles for binding monovalent cations. The particles have a nucleus and a coating; the nucleus contains a cation exchange material and the coating comprises a membrane that is permeable for monovalent cations. This coating is disclosed as being more permeable for monovalent cations than for bi- or higher valent cations. Exemplified cation exchange materials are polyphosphate and polystyrene sulfonate resins. Exemplified coatings are cellulose acetate and crosslinked polyethyleneimine. Generally, these particles are disclosed for treating hypertension. The polyethyleneimine shells of Notenbomer do not contain repeat units derived from an acrylic, methacrylic, styrenic, dienic, or vinylic monomer because they are prepared by ring opening polymerization of ethylene imine having the following structure.

Ethylene imine is not an acrylic (H_2C=C(R)-C(O)-R), methacrylic (H_2C=$C(CH_3)$-C(O)-R), styrenic (C_6H_5-C(R)=CH_2), dienic (CH_2=C(R)-R-C(R)=CH_2), or vinylic (R-C(R)=CH_2) monomer[2] because it does not contain a double bond as required for all the members of the Markush group. Further, the polyethyleneimine shell of Notenbomer contains a nitrogen atom in the backbone of the polymer whereas the polymer shell of claim 1 contains only carbon atoms in

[2] Note that R in these monomers can independently be various substituents as known in the art. The formulae are presented to support the difference in the monomer structures as compared to ethylene imine.

the backbone of the polymer. Thus, Notenbomer does not describe all the elements of claim 1 because it does not describe a shell component comprising crosslinked polymer coatings containing repeat units derived from acrylic, methacrylic, styrenic, dienic, vinylic monomers that result in polymer shells containing only carbon atoms in the polymer backbone as required by claim 1. Thus, claims 1, 10, 16, 17, 20, 21, 23, 31, 32, 46-50, 54, 57-63, and 69 are not anticipated by Notenbomer (EP 0 730 494) under 35 U.S.C. § 102(b).

35 U.S.C. § 103 Rejections

Applicants submit that the rejections under 35 U.S.C. § 103 addressed below are in error for the following reasons.

Legal Framework

Initially, the determination of whether a claim is obvious under 35 U.S.C. § 103 depends on at least four underlying factual issues set forth in *Graham v. John Deere Co. of Kansas City*[3]: (1) the scope and content of the prior art; (2) differences between the prior art and the claims at issue; (3) the level of ordinary skill in the pertinent art; and (4) evaluation of any relevant secondary considerations. In April 2007, the Supreme Court affirmed the *Graham* analysis as the framework for determining obviousness.[4]

In addressing the scope and content of the prior art, references are not pertinent to an obviousness inquiry if they are not from analogous art.[5] A reference is analogous art if: (1) the reference is from the same field of endeavor, regardless of the problem addressed, or (2) the reference is not within the inventor's field of endeavor, yet it is reasonably pertinent to the particular problem addressed by the inventor. In *Clay*, the PTO asserted that the claimed invention and the Sydansk reference were part of a common endeavor of "maximizing withdrawal of petroleum stored in petroleum reservoirs."[6] Sydansk taught the

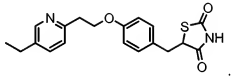
[3] 383 U.S. 1, 17, 86 S.Ct. 684, 15 L.Ed.2d 545 (1966).
[4] *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1739 (2007).
[5] *In re Clay*, 23 U.S.P.Q.2d 1058, 1060 (Fed. Cir. 1992).
[6] *Id.*

> use of a gel in unconfined and irregular volumes within generally underground natural oil-bearing formation to channel flow in a desired direction; Clay teaches the introduction of gel to the confined dead volume of a man-made storage tank.[7]

However, the Federal Circuit disagreed with the Office and held that Clay's field of endeavor was "*storage* of refined liquid hydrocarbons" and Sydansk's invention was directed to the "*extraction* of crude petroleum."

The second step of the *Graham* analysis requires consideration of the differences between the prior art and the claims at issue. It is well established law, that, where, as here, the patent at issue claims a chemical compound, the analysis of the *Graham f*actor i.e., the differences between the claimed invention and the prior art, often turns on the structural similarities and differences between the claimed compound and the prior art compounds.[8] Obviousness based on structural similarity thus can be proved by identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (i.e. a lead compound) in a particular way to achieve the claimed compound.[9]

In *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*,[10] the Federal Circuit addressed the obviousness issue for structurally similar chemical compounds. In *Takeda*, the claim at issue recited pioglitazone (5-{4-[2-(5-ethyl-2-pyridyl)ethoxy] benzyl}-2,4-thiazolidinedione) having the following structure:



The ethyl substituent is attached to the 5-position on the pyridyl ring.

Alphapharm filed an ANDA to manufacture and sell a generic version of pioglitazone. According to Alphapharm, Takeda's claimed compound would have been obvious over the prior art compound TZD ("compound b": a pyridyl ring with a methyl (CH_3) group attached to the 6-position of the ring),[11] having the following structure:

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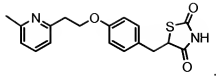
[7] *Id.*
[8] *See Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.*, 471 F.3d 1369, 1377; 81 USPQ2d 1324 (Fed. Cir. 2006).
[9] *See Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356; 83 USPQ2d 1169 (Fed. Cir. 2007).
[10] 492 F.3d 1350 (Fed. Cir. 2007).
[11] *Id.* at 1354.



Alphapharm argued that one of ordinary skill in the art would select compound b for antidiabetic research and then make "two obvious chemical changes: first, homologation, i.e., replacing the methyl group with an ethyl group, which would have resulted in a 6-ethyl compound; and second, 'ring-walking,' or moving the ethyl substituent to another position on the ring, the 5-position, thereby leading to the discovery of pioglitazone."[12]

The district court found, however, that one of ordinary skill in the art would not have selected compound b from the "hundreds of millions" of possible compounds. "[T]he prior art did not suggest to one of ordinary skill in the art that compound b would be the best candidate as the lead compound for antidiabetic research."[13] The Federal Circuit affirmed and held that there was no motivation to select a particular prior art compound (e.g., compound b) from the universe of prior art compounds and even if there was such a motivation, nothing in the prior art would have led a skilled person to modify compound b to arrive at the claimed compound. Thus, when determining the obviousness of new chemical compounds, there must be "some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness."[14]

Once a reason to modify a known compound is found, the skilled person must also have a reasonable expectation that such a modification will be successful or beneficial in some way. In many chemical cases a "reasonable expectation of success" is not always found, as the Federal Circuit stated in *Eisai Co. v. Dr. Reddy's Laboratories, Inc.*[15] :

> First, KSR assumes a starting reference point or points in the art, prior to the time of invention, from which a skilled artisan might identify a problem and pursue potential solutions. Second, KSR presupposes that the record up to the time of invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound. See Takeda Chem. Indus. v. Alphapharm Pty., Ltd., 492 F.3d 1350, 1356 (Fed. Cir. 2007). ("Thus, in cases involving new chemical compounds, it remains necessary

[12] *Id.* at 1357.
[13] *Id.* at 1358.
[14] *Id.*
[15] *Eisai Co. v. Dr. Reddy's Laboratories, Inc.*, 87 U.S.P.Q.2d 1452 (Fed. Cir. 2008).

> to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound."). Third, the Supreme Court's analysis in KSR presumes that the record before the time of invention would supply some reasons for narrowing the prior art universe to a "finite number of identified, predictable solutions," 127 S. Ct. at 1742. In Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc., 520 F.3d 1358, 1364 (Fed. Cir. 2008), this court further explained that this "easily traversed, small and finite number of alternatives . . . might support an inference of obviousness." To the extent an art is unpredictable, as the chemical arts often are, KSR's focus on these "identified, predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable. (Emphasis added)

Notenbomer in view of Cohen

Reconsideration is respectfully requested of the rejection of claims 1, 10, 16, 17, 20-24, 31, 32, 46-50, 54-63, and 67-69 as unpatentable over Notenbomer (EP 0 730 494) in view of Cohen et al. (U.S. Patent No. 6,558,665) under 35 U.S.C. § 103(a). Claim 1 and Notenbomer are described above in connection with the 35 U.S.C. § 102 rejection. The Office states that it "would have been obvious to coat the particles of the '494 patent in a similar fashion of the '665 patent since they both use the same method to apply uniform coatings."[16]

Cohen et al. describes methods of coating particles with a coating of uniform thickness that conforms to the size and shape of the particles. In particular, the particles coated are islet cells that are used to treat diabetes. The particles can be coated with poly(ethylene glycol) or poly(oxyethylene)-poly(oxypropylene) block copolymers. The islet cells are coated to provide "immunoisolation of the cell by providing a semi-permeable barrier between the host and the transplanted tissue."[17]

In *Clay*, the PTO asserted that the claimed invention and the Sydansk reference were of a common endeavor because they were directed to "maximizing withdrawal of petroleum stored in petroleum reservoirs."[18] In this case, the PTO provides no reason why the Cohen patent is analogous art to either the invention or Notenbomer, but does state that the reason the Cohen patent and the Notenbomer patent can be combined is because "they both use the same method to

[16] See Office action dated March 5, 2009 at page 9.
[17] See U.S. Patent No. 6,558,665 at column 8, lines 26-28.
[18] *Id.*

apply uniform coatings."[19] However, Applicants' endeavor is development of oral potassium binders.[20] The Cohen patent is directed to methods of coating particles in order to develop coated islet cells for treating diabetes that are not rejected by the host. Thus, Applicants submit that a skilled person would not have looked to the Cohen patent when developing oral core-shell potassium binders because Cohen is not in Applicants' field of endeavor nor does it address a problem disclosed in either applicants' specification or the Notenbomer patent.

For argument's sake, if Notenbomer and Cohen could be properly combined, the second step of the *Graham* analysis requires consideration of the differences between the prior art and the claims at issue. The Notenbomer patent discloses core-shell particles having shells that are more permeable to monovalent ions than divalent ions. Notenbomer does not disclose core-shell particles having shells containing repeat units derived from acrylic, methacrylic, styrenic, dienic, or vinylic monomers. Cohen describes particles having coatings of poly(ethylene glycol) or poly(oxyethylene)-poly(oxypropylene) block copolymers, which are polymers derived from polymerization of ethylene oxide or propylene oxide.

ethylene oxide

propylene oxide

These polymers are <u>not</u> polymers containing repeat units derived from acrylic, methacrylic, styrenic, dienic, or vinylic monomers. The Cohen coatings are polymers containing an oxygen atom in the backbone of the polymer while the monomers of claim 1 produce polymers containing only carbon atoms in the backbone of the polymer. Thus, the <u>difference</u> between the instant claims and the combination of the Notenbomer and Cohen patents is that the instant claims require shells that are crosslinked polymers containing repeat units derived from acrylic, methacrylic, styrenic, dienic, or vinylic monomers and the cited references do not include that element. Thus, the combination of the cited references does not include all the elements.

[19] See Office action dated March 5, 2009 at page 9.
[20] See specification at paragraph [0019] and original claim 43.

Moreover, for argument's sake, just like Alphapharm in *Takeda*, the PTO is arguing that it would have been obvious to one of ordinary skill in the art to choose the specific polymeric coatings in Cohen from millions of possible available coatings in the prior art because the coating methods were the same. As *KSR v. Teleflex* and *Takeda v. Alphapharm* emphasize, it is important to "identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does."[21] Although the Office states that the similar coating methods would be the reason for combining the references, similar to *Ex parte Meagher*, such a general statement for the reason for combining the references does not indicate why one would select the Cohen patent from the multitude of references describing the same coating method.[22] Further, there is no reason provided in the cited art or reliance on knowledge in the art that would have led a skilled person to select the Cohen patent or poly(ethylene glycol) or poly(oxyethylene)-poly(oxypropylene) block copolymers to modify the core-shell particles of the Notenbomer patent. Not only is there no reason to combine the teaching of a poly(ethylene glycol) or poly(oxyethylene)-poly(oxypropylene) block copolymer coating from the Cohen patent, the Cohen patent cannot properly be combined with the Notenbomer patent because the two patents are not in the same field of endeavor and do not address the same problem, so they are not analogous art. The PTO has failed to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed invention does. There is simply no reason that a skilled person would have combined the Notenbomer and Cohen patents to arrive at the claimed invention.

Applicants submit that the PTO is engaging in the exact hindsight bias that the Court has repeatedly urged must be avoided. The PTO has not provided a reason why a skilled person would choose the coatings of poly(ethylene glycol) or poly(oxyethylene)-poly(oxypropylene) block copolymer as described in the Cohen patent. Hence, the only way that the PTO could

[21] *KSR v. Teleflex, Inc.*, 82 U.S.P.Q.2d 1385, 1396.

[22] *Ex parte Meagher*, Appeal no. 2008-3613; Application No. 10/380,898 decided September 22, 2008 at page 15 (describing that combining references for the purpose of "obtaining a conversion coating having good corrosion resistance and good top coat adhesion properties-which are likely goals of virtually every conversion coating composition-do not provide the ordinary coating formulations chemist with a reason to systematically vary" the prior art compositions to arrive at the claimed composition.).

arrive at this conclusion is based on the teachings of the instant application while disregarding what the art would have actually led a skilled person to do.

Claim 68 is directed to an oral pharmaceutical composition comprising a pharmaceutically acceptable excipient and core-shell particles. These core-shell particles comprise a core component and a shell component. The core component comprises a potassium-binding cation exchange polymer. The shell component comprises a crosslinked polymer produced by polymerization of an acrylic or methacrylic monomer wherein the shell component is about 0.005 microns to about 20 microns thick and the core-shell particle size is about 200 nm to about 2 mm. The shell component is essentially not disintegrated during residence and passage through the gastro-intestinal tract of an animal subject. Claims 68 and 69 are patentable over Notenbomer in view of Cohen for at least the same reasons described above. Additionally, claim 68 requires the shell to contain polymers derived from acrylic or methacrylic monomers. Since neither Notenbomer nor Cohen describe shell polymers derived from acrylic or methacrylic monomers, all the elements of claim 68 are not disclosed by the combined references.

In sum, claims 1, 10, 16, 17, 20-24, 31, 32, 46-50, 54-63, and 67-69 are patentable over Notenbomer (EP 0 730 494) in view of Cohen et al. (U.S. Patent No. 6,558,665) under 35 U.S.C. § 103(a).

Notenbomer in view of Chong

Reconsideration is respectfully requested of the rejection of claim 45 as unpatentable over Notenbomer (EP 0 730 494) in view of Chong et al. (U.S. Patent No. 4,389,590) under 35 U.S.C. § 103(a). Claim 45 is directed to a method of removing potassium ion from a gastrointestinal tract of an animal subject in need thereof and suffering from renal insufficiency or renal failure. The method comprises administering to the animal subject a composition comprising core-shell particles. The core-shell particles comprise a core component and a shell component wherein the core component comprises a potassium-binding cation exchange polymer and the shell component comprises a polymer being produced by free radical polymerization of an ethylenic monomer. The core-shell particles bind potassium ion in the gastrointestinal tract of the animal subject and retain bound potassium ion with the core-shell particles during residence and passage of the core-shell particles through the gastro-intestinal

tract of the animal subject whereby potassium ion is removed from the gastrointestinal tract of the animal subject by the core-shell particles to obtain a therapeutic and/or prophylactic benefit.

Notenbomer is described above in connection with the 35 U.S.C. § 102 rejection. Chong et al. (the '590 patent) describe liquid cation exchange materials comprising emulsions of submicroscopic, spherical beads having diameters from about 0.01 to about 1.5 microns and having from about 0.7 to about 1.5 cation exchange functional groups per monomer unit wherein the cation exchange functional groups are strong acid groups or free acid forms of weak acid groups. The reference further describes that strongly acidic resins in the sodium form can be used for treating hyperkalemia. The Office asserts that from the "suggestion of the '590 patent to use acid cation ion exchange resins to treat hyperkalemia, the artisan of ordinary skill would have been motivated to apply the composition of the '494 patent in order to remove excess potassium ions from the body effectively treating hyperkalemia in a human patient in need of treatment."[23]

However, Chong et al. do not describe any shell materials, is directed to preparing small particle size, spherical ion exchange resins, and is only cited for the disclosure that strongly acidic resins in the sodium form can be used for treating hyperkalemia. Thus, Chong is not properly combined with Notenbomer because Chong is not directed to the problem of claim 45 or of Notenbomer.

Moreover, the Office ignores the requirement that the patient is suffering from renal insufficiency or renal failure and asserts that this limitation is merely a future intended use for the dosage form.[24] In *Jansen v. Rexall Sundown, Inc.*,[25] a claim directed to a "method of treating or preventing macrocytic-megaloblastic anemia in humans" by "administering a ... vitamin preparation to a human in need thereof...."[26] was construed by the Federal Circuit as follows.

> [T]he claims' recitation of a patient or a human "in need" gives life and meaning to the preambles' statement of purpose. *See Kropa v. Robie*, 187 F.2d 150, 152 [88 U.S.P.Q. 478] (C.C.P.A. 1951) (stating the rule that a preamble is treated as a limitation if it gives "life and meaning" to the claim). The preamble is therefore not merely a statement of effect that may or may not be desired or

[23] See page 12 of Office action dated March 5, 2009.
[24] See page 10 of Office action dated March 5, 2009.
[25] 68 U.S.P.Q.2d 1154, 1158 (Fed. Cir. 2003).
[26] See id. at 1155.

> appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed.[27]

Thus, the preamble's requirement that the core-shell particles be administered to a patient suffering from renal insufficiency or renal failure is an element that must be present in the cited references in order to negate patentability of claim 45.

Since the preamble must be given patentable weight, the issue is whether it would have been obvious from the cited references to treat a patient suffering from renal insufficiency or renal failure with core-shell particles having a shell comprising crosslinked polymers containing repeat units derived from ethylenic monomers. There can be no basis for inherency where the claim is directed to a method of treating a condition that ordinarily would not have been present in the patients whose treatment is described in the prior art; and there can be no basis for obviousness where the prior art further fails to recognize the potential effect of the treating agent against the condition specified in the claim. As the C.C.P.A has stated in reversing an obviousness rejection of a claim to a method of treating a specified condition with a defined treatment agent based on the inherent effect of treating a different condition with a similar agent:

> [Inherency] is quite immaterial if, as the record establishes here, one of ordinary skill in the art would not appreciate or recognize that inherent result, *in re Shetty*.[28]

The method claims at issue in *Shetty* were directed to methods for appetite control and the cited prior art disclosed compounds and dosages useful for combating microbial infestation. The *Shetty* court stated that the Office had "failed to show a reasonable expectation, or some predictability" that the prior art compound disclosed in the first reference would be an effective appetite suppressant if administered in the dosage disclosed in the second reference and that the Office's hindsight assertion that the dosages would make the weight loss method obvious was insufficient.[29] Similar to *Shetty*, claim 45 recites a method for removing potassium in a patient in need thereof and suffering from renal insufficiency or renal failure by administering core-shell particles having a shell of crosslinked polymers containing repeat units derived from ethylenic monomers while Chong discloses that its resins can be used for treating hyperkalemia and

[27] See id. at 1158.
[28] 195 U.S.P.Q. 753.
[29] See id. at 756.

Notenbomer discloses methods for treating hypertension by administration of core-shell particles. Thus, claim 45 is patentable over the cited references.

Moreover, the court in *Ex parte Zbornik* found a process for treating Air Sac Infection in fowl patentable over prior art disclosing substantially the same compound to treat ducks for malaria.[30] The *Zbornik* court found that the claims were patentable because the cited reference was not concerned with appellant's problem and it failed to suggest its solution. Similarly, the cited references are concerned with preparing small particle diameter ion exchange resins and treating hypertension by administration of core-shell particles, and they fail to suggest to a skilled person that the claimed core-shell particles would have been beneficial to remove potassium from a patient in need thereof and suffering from renal insufficiency and renal failure.

In sum, claim 45 is patentable in view of the cited references.

Notenbomer in view of Shimizu et al. and Macek et al.

Reconsideration is respectfully requested of the rejection of claims 1, 51-53, 62, 64, and 65 as unpatentable over Notenbomer (EP 0 730 494) in view of Shimizu et al. (U.S. Patent No. 5,824,339) and Macek et al. (U.S. Patent No. 3,499,960) under 35 U.S.C. § 103(a). Claim 1 is described in detail above, claims 51-53, 64, and 65 further require specific ethylenic monomers. The Office asserts that it would have been obvious "to combine the teachings and suggestions with an expected result of a palatable oral formulation useful in the treatment of a variety of ion related disorders."[31]

Notenbomer is described above in connection with the 35 U.S.C. § 102 rejection. Shimizu et al. disclose drug delivery systems of effervescent compositions of core-shell powders having a fine granular core spray-coated with a liquid mixture containing a water-soluble polymer, a physiologically active substance, and an enteric coating. Further, Shimizu et al. disclose water-soluble polymers of hydroxypropylcelluose (HPC), polyvinylpyrrolidone, hydroxypropylmethylcellulose (HPMC), methylcellulose, carboxymethylcellulose sodium, sodium polyacrylate, polyvinylalcohol, sodium alginate, guar gum, etc.[32] For use as an enteric coating, Shimizu discloses cellulose acetate phthalate (CAP), hydroxypropylmethylcellulose

[30] *Ex parte Zbornik*, 109 U.S.P.Q. 508.
[31] See page 13 of Office action dated March 5, 2009.
[32] See U.S. Patent No. 5,824,339 at column 4, lines 40-46.

phthalate (HP-55), hydroxymethylcellulose acetate succinate, acrylic copolymers (e.g. Eudragit L30D-55), carboxymethylethylcellulose, and shellac.[33]

Macek et al. disclose polymers used to remove bile acids; the polymers disclosed are polystyrene resins crosslinked with divinyl benzene and functionalized through chloromethylation of the aromatic rings and replacement of the chlorine atom with a tertiary amine such as trimethyl amine to form a trimethyl ammonium group attached to the aromatic rings. Thus, the polymers are amine polymers that can be coated with carboxypolymethylene crosslinked with polyallyl sucrose or an acrylic acid polymer crosslinked with polyallylsucrose.

Similar to Alphapharm in *Takeda*, the PTO is arguing that it would have been obvious to one of ordinary skill in the art to choose the specific polymeric coatings in Shimizu and Macek from millions of possible available coatings "in order to provide sufficient permeability of potassium ions into the cation exchange core"[34] of the Notenbomer particles. As *KSR v. Teleflex* and *Takeda v. Alphapharm* emphasize, it is important to "identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does."[35] Although the Office states that the palatable oral formulations would be the reason for combining the references, similar to *Ex parte Meagher*, such a general statement for the reason for combining the references is likely the goal of every reference concerned with coated pharmaceutical particles for oral administration. Further, there is no reason provided in the cited art or reliance on knowledge in the art that would have led a skilled person to select the coatings of Shimizu or Macek to modify the core-shell particles of the Notenbomer patent. For example, Shimizu and Macek are directed to different problems than Notenbomer or the claimed invention. Notenbomer and the claimed invention are directed to core-shell particles for binding potassium. In contrast, Shimizu is directed to effervescent compositions that provide delayed release of the active agent and disclose shell polymers that are water soluble. Thus, since the problem of Shimizu is different from Notenbomer's, not only is it not properly combined with Notenbomer, but it does not provide a reasonable expectation that the modified particles would have the claimed elements including shell nondisintegration. Further, Macek is directed to bile acid binders that have a core of an amine polymer and a shell

[33] See U.S. Patent No. 5,824,339 at column 7, lines 17-21.
[34] See page 13 of Office action dated March 5, 2009.
[35] *KSR v. Teleflex, Inc.*, 82 U.S.P.Q.2d 1385, 1396.

that can be an acrylic acid polymer and provides a palatable composition. An amine polymer core binds anions (e.g., bile acids) and would not be a potassium binding cation exchange polymer as required by the instant claims.

Therefore, the PTO has failed to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed invention does. There is simply no reason that a skilled person would have combined Notenbomer and the Shimizu and Macek patents to arrive at the claimed invention. Applicants submit that the PTO is engaging in the very hindsight bias that the Court has repeatedly urged must be avoided. The PTO has not provided a reason why a skilled person would have chosen the coatings of Shimizu or Macek from the universe of possible coatings. Hence, the only way that the PTO could arrive at this conclusion is based on the teachings of the instant application while disregarding what the art would have actually led a skilled person to do. Thus, claims 1, 51-53, 62, 64, and 65 are patentable over Notenbomer (EP 0 730 494) in view of Shimizu et al. (U.S. Patent No. 5,824,339) and Macek et al. (U.S. Patent No. 3,499,960) under 35 U.S.C. § 103(a).

CONCLUSION

Applicant submits that the present application is now in condition for allowance and requests early allowance of the pending claims.

The Commissioner is hereby authorized to charge any under payment or credit any over payment to Deposit Account No. 19-1345.

Respectfully submitted,

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JSH/clp